

normal range. In addition, plasma levels of the two proteins are more strikingly elevated in patients with deep venous thrombosis, pulmonary embolism, arterial occlusion and myocardial infarction. Finally, PF4 and  $\beta$ TG are elevated in patients during episodes of spontaneous and exercise-induced myocardial ischemia and angina pectoris. Thus, an increased plasma level can signify platelet activation in chronic vascular disease or in acute ischemia and thrombosis. Although there is a close correlation, the tests do not distinguish between a primary and secondary platelet role in these diseases.

There are also some serious technical limitations to these assays. For example, it is not yet clear which of the protein measurements provides the best estimate of in vivo platelet activation. Because  $\beta$ TG is cleared and metabolized by the kidney, renal failure increases the plasma level of  $\beta$ TG without any activation of the coagulation system. PF4 might seem to be a superior marker because its plasma level is not influenced by renal function. However, it adheres to endothelial cells lining blood vessels and can be displaced by the administration of therapeutic concentrations of heparin.<sup>5</sup> While the presence of PF4 on vascular endothelium may have biological importance and may, in fact, modulate coagulation reactions, this interaction complicates the interpretation of plasma radioimmunoassays. To circumvent these problems, some investigators have suggested that both PF4 and  $\beta$ TG should be measured simultaneously and that a high ratio of  $\beta$ TG to PF4 would reflect in vivo release, whereas a ratio that approximates their content in platelets might represent release in vitro. Interestingly, in most clinical reports, plasma levels of both proteins rise in parallel.

Given these uncertainties, can such tests be applied clinically? If clinical application means ordering a battery of radioimmunoassays to diagnose early vascular disease or to predict impending thrombosis, the answer is probably no. However, techniques that can measure secreted platelet proteins and activation products or complexes formed during the coagulation process are valuable tools for clinical investigation. The assays should permit studies with human subjects that have previously been possible only with purified protein mixtures in vitro. For example, it should now be possible to determine (1) if coagulation reactions proceed in vivo by the pathways postulated from experiments in test tubes, (2) if there are patients in

whom there is evidence for activation of coagulation before clinical thromboembolism (hypercoagulable state), (3) if the tests change in a predictable manner during acute thrombotic events and (4) if they can be used to monitor the efficacy of antithrombotic therapy.

It is hoped that the answers to these questions, as well as many other unforeseen ones, will soon become available. It may then be possible for clinicians to identify patients with a predisposition to thrombosis and then prescribe appropriate therapy. Radioimmunoassays of the coagulation system could then become as useful as their endocrine counterparts. However, only with more knowledge of the progression of such illnesses and the effect of therapy, both on the clinical outcome and the laboratory tests, will it be possible to predict the usefulness of these tests. For practicing physicians, the best approach, for the moment, may be to watch and wait. It should be remembered that, in medicine as in other human endeavors, "Time cools, time clarifies. . . ."<sup>6</sup>

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## Adoption and Freedom of Information

ELSEWHERE IN THIS ISSUE Davis and Brown discuss changing attitudes and circumstances with respect to adoptions. Of particular interest is the fairly recent trend toward what might be called freedom of information among what is called the "adoption triangle"—that is, the true parents, the adopted child and the adoptive parents. A case is made that, for all concerned, knowing is better than not knowing and that physicians should do what they can to facilitate the exchange of information, whether in the care of their patients or by

acting as advocates in the community or for legislation.

In one sense this changing attitude may be viewed as a response to a loss which is shared by each part of the triangle as suggested by the authors, but it may also be an expression of a growing distrust of any practice which conceals information about a person from that person whether legally or otherwise. In any case it is always wise to ask why things got to be the way they are in the first place. There is always a reason, one which may or may not any longer be valid. This writer has a lurking feeling that a genuine maturity on the part of all the persons concerned may be necessary before all information can be exchanged without danger of harm to someone, and this may be a reason things got to be the way they are—that is, with safeguards. Genuine maturity is often not a characteristic of all the parties in the adoption triangle at the time of the adoption, and there is a primary responsibility to protect the interests of the adopted person, especially if a child.

—MSMW

## Diet, Serum Cholesterol and Coronary Heart Disease *Has the Dilemma Been Resolved at Last?*

THE DEBATE as to whether dietary quality and quantity is causally related to atherosclerosis has raged on for decades. As soon as a consensus appears to have been reached, foes of that consensus seem quick to publish recommendations based on the opposite conclusion. Most recently these have come from the skeptics (or nihilists, some would contend). First, an article by George Mann was published in the *New England Journal of Medicine*<sup>1</sup> entitled "Diet-Heart: End of an Era," and just last year the report of the Food and Nutrition Board of the National Research Council appeared.<sup>2</sup> Predictably, both of these reports, which concluded that insufficient evidence linking diet with coronary disease had been gathered on which to base recommendations for a change in national diet patterns, generated rebuttal which far outweighed the original reports.

Now that the brouhaha which followed the latter report has begun to abate (much of which took an unfortunate and unwarranted tone), we find the pendulum of fact and opinion swinging

back toward that supported by the scientific establishment. That movement received substantial support in the recent report from the Chicago Western Electric Study,<sup>3</sup> which linked not only serum cholesterol with coronary risk in middle-aged men, a well-established association, but also, for the first time in an American multiethnic study, demonstrated a positive association between a score summarizing each participant's dietary intake of cholesterol and saturated and polyunsaturated fatty acids with their serum cholesterol level at the initial examination, a correlation between subsequent change in that score and change in serum cholesterol, and a significant relationship between the mean base-line diet score and the 19-year risk of death from coronary heart disease. The authors noted that conclusions from their study, if viewed in isolation, would be limited; when viewed in the context of the accumulated literature on the subject, however, their findings were interpreted to support the contention that dietary lipid composition affects not only the level of serum cholesterol but also, more important, the long-term risk of death from coronary heart disease in middle-aged American men.

A similar conclusion is reached in the article by Hulley and his co-workers, which appears elsewhere in this issue. As they have attempted with other controversial topics (for example, the relationship of serum triglycerides to coronary risk<sup>4</sup>), these authors have assessed the total literature to reach a strong conclusion, in this instance that "it is certain that dietary fats influence the level of serum cholesterol, and that it is highly likely that serum cholesterol is a cause of atherosclerosis and coronary heart disease." They then give broad guidelines for an approach to dietary intervention and estimate the resulting magnitude of reduction in coronary heart disease risk. (Parenthetically, experience and common sense challenge their calculated reduction in cholesterol. The total decrease of 140 mg per dl from all of the modifications illustrated is clearly not possible [and probably not desirable] in a person with a median cholesterol level of 213 mg per dl.) In short, despite their admission that the evidence linking dietary fats to coronary heart disease is largely circumstantial, they conclude that it is time to settle the matter and contend that their method of analysis has done just that.

But has it? We agree that more convincing findings are not likely to be forthcoming in the near future and that the essence of wisdom (and the